

deleted from a first sequence region in the [comprising an] the N-terminal 378 amino acids [region that comprises a first sequence region from which at least one amino acid has been deleted].

4 (once amended). The DNA segment of claim 3, wherein at least [about] 25 amino acids have been deleted from said first sequence region.

5 (once amended). The DNA segment of claim 4, wherein at least [about] 100 amino acids have been deleted from said first sequence region.

6 (once amended). The DNA segment of claim 5, wherein at least [about] 150 amino acids have been deleted from said first sequence region.

7 (once amended). The DNA segment of claim 6, wherein at least [about] 300 amino acids have been deleted from said first sequence region.

8 (once amended). The DNA segment of claim 2, wherein said first sequence region is located:

- a) between [about] amino acid 1 and [about] amino acid 50;
- b) between [about] amino acid 51 and [about] amino acid 100;
- c) between [about] amino acid 101 and [about] amino acid 150;
- d) between [about] amino acid 151 and [about] amino acid 200;
- e) between [about] amino acid 201 and [about] amino acid 250;
- f) between [about] amino acid 251 and [about] amino acid 300;
- g) between [about] amino acid 1 and [about] amino acid 100;
- h) between [about] amino acid 51 and [about] amino acid 150;
- i) between [about] amino acid 101 and [about] amino acid 200;
- j) between [about] amino acid 151 and [about] amino acid 250;
- k) between [about] amino acid 201 and [about] amino acid 300;
- l) between [about] amino acid 1 and [about] amino acid 150;
- m) between [about] amino acid 51 and [about] amino acid 200;
- n) between [about] amino acid 101 and [about] amino acid 250;
- o) between [about] amino acid 151 and [about] amino acid 300;
- p) between [about] amino acid 1 and [about] amino acid 200;
- q) between [about] amino acid 51 and [about] amino acid 250;
- r) between [about] amino acid 101 and [about] amino acid 300;
- s) between [about] amino acid 1 and [about] amino acid 250;

- t) between [about] amino acid 51 and [about] amino acid 300; or
  - u) between [about] amino acid 1 and [about] amino acid 300.
- 9 (once amended). The DNA segment of claim 2, wherein:
- a) [about] amino acid 2 through [about] amino acid 34 have been deleted from said first sequence region;
  - b) [about] amino acid 2 through [about] amino acid 55 have been deleted from said first sequence region;
  - c) [about] amino acid 2 through [about] amino acid 78 have been deleted from said first sequence region;
  - d) [about] amino acid 2 through [about] amino acid 97 have been deleted from said first sequence region;
  - e) [about] amino acid 2 through [about] amino acid 148 have been deleted from said first sequence region;
  - f) [about] amino acid 31 through [about] amino acid 107 have been deleted from said first sequence region;
  - g) [about] amino acid 77 through [about] amino acid 107 have been deleted from said first sequence region;
  - h) [about] amino acid 111 through [about] amino acid 181 have been deleted from said first sequence region;
  - i) [about] amino acid 111 through [about] amino acid 241 have been deleted from said first sequence region;
  - j) [about] amino acid 181 through [about] amino acid 241 have been deleted from said first sequence region; or
  - k) [about] amino acid 242 through [about] amino acid 300 have been deleted from said first sequence region.

10 (once amended). The DNA segment of claim 2, wherein at least one amino acid has been deleted from said [N-terminal region of said] modified retinoblastoma tumor suppressor protein [further comprises] in a second sequence region different from the first sequence region [which at least one amino acid has been deleted].

11 (once amended). The DNA segment of claim 10, wherein [about] amino acid 2 through [about] amino acid 34, and [about] amino acid 76 through [about] amino acid 112 have been deleted.

12 (once amended). The DNA segment of claim 10, wherein [about] amino acid 2 through [about] amino acid 55, and [about] amino acid 76 through [about] amino acid 112 have been deleted.

13 (once amended). The DNA segment of claim 1, wherein said gene encodes a modified retinoblastoma tumor suppressor protein [comprising at least a first N-terminal mutation, and wherein said modified retinoblastoma tumor suppressor protein] that has an increased biological activity in comparison to the biological activity of the corresponding wild-type retinoblastoma tumor suppressor protein.

14 (once amended). The DNA segment of claim 13, wherein said gene encodes a modified retinoblastoma tumor suppressor protein comprising a substitution mutation at position 111.

16 (once amended). The DNA segment of claim 13, wherein said modified retinoblastoma tumor suppressor protein comprises at least a second insertion, substitution or deletion within [in] the N-terminal 378 amino acids [mutation].

17 (once amended). The DNA segment of claim 16, wherein said gene encodes a modified retinoblastoma tumor suppressor protein comprising a substitution mutation at position 111 and a substitution mutation at position 112.

19 (once amended). The DNA segment of claim 1, wherein said gene encodes a modified retinoblastoma tumor suppressor protein [comprising an N-terminal region from] in which at least one amino acid has been deleted, and in which [contains] at least one amino acid has been substituted [mutation].

20 (once amended). The DNA segment of claim 2, wherein said gene encodes a modified retinoblastoma tumor suppressor protein that comprises at least the C-terminal amino acid sequence from [about position] amino acid 370 to [about position] amino acid 928 of SEQ ID NO:2.

21 (once amended). The DNA segment of claim 2, wherein said gene encodes a modified retinoblastoma tumor suppressor protein [comprising] consisting of the contiguous amino acid sequence of SEQ ID NO:29; SEQ ID NO:31; SEQ ID NO:33; SEQ ID NO:35; SEQ ID NO:37; SEQ ID NO:39; SEQ ID NO:41; SEQ ID NO:43; SEQ ID NO:45; SEQ ID NO:47; SEQ ID NO:49; or SEQ ID NO:51.

22 (once amended). The DNA segment of claim 2, wherein said gene consists of [comprises] the contiguous nucleic acid sequence from between position 7 and position

2691 of SEQ ID NO:28; from between position 7 and position 2628 of SEQ ID NO:30; from between position 7 and position 2559 of SEQ ID NO:32; from between position 7 and position 2502 of SEQ ID NO:34; from between position 7 and position 2349 of SEQ ID NO:36; from between position 7 and position 2559 of SEQ ID NO:38; from between position 7 and position 2697 of SEQ ID NO:40; from between position 7 and position 2583 of SEQ ID NO:42; from between position 7 and position 2397 of SEQ ID NO:44; from between position 7 and position 2613 of SEQ ID NO:46; from between position 7 and position 2619 of SEQ ID NO:48; or from between position 7 and position 2790 of SEQ ID NO:50.

23 (once amended). The DNA segment of claim 1, operationally [positioned] linked under the control of a promoter.

24 (once amended). The DNA segment of claim 23 [, further defined as] contained within a recombinant vector.

25 (once amended). The DNA segment of claim 24, wherein said recombinant vector is [comprised] contained within an adenoviral vector.

26 (once amended). The DNA segment of claim 25, wherein said adenoviral vector is [comprised] contained within a recombinant adenovirus.

27 (once amended). The DNA segment of claim 1, recombinantly transformed [comprised within] into a host cell.

34 (once amended). The DNA segment of claim 1, wherein said gene encodes a modified retinoblastoma tumor suppressor protein [is characterized as]:

- a) comprising [an] at least one amino acid deletion in the N-terminal 378 amino acids [region that comprises at least a first sequence region from which at least one amino acid has been deleted], and wherein said modified retinoblastoma tumor suppressor protein has a biological activity at least [about] equivalent to the biological activity of the corresponding wild-type retinoblastoma tumor suppressor protein; or
- b) comprising [an] at least one insertion or substitution in the N-terminal 378 amino acids [region that comprises a first sequence region comprising at least one mutation], and wherein said modified retinoblastoma tumor suppressor protein has an increased biological activity in comparison to the biological activity of the corresponding wild-type retinoblastoma tumor suppressor protein.

36 (once amended). A recombinant host cell comprising a DNA segment comprising an isolated gene encoding a modified retinoblastoma tumor suppressor protein other than pRB<sup>94</sup> or pRB<sup>56</sup>, in which said modified retinoblastoma tumor suppressor protein [comprising] comprises an insertion, substitution or deletion within the N-terminal 378 amino acids of said protein [modification], with the proviso that said modified protein does not comprise a deletion of amino acids 1 through 378, which modified retinoblastoma protein has a biological activity at least equivalent to the biological activity of the corresponding wild type retinoblastoma protein.

Please add the following claims:

44 (new). A DNA segment comprising an isolated gene encoding for a modified retinoblastoma tumor suppressor protein, wherein said gene consists of the contiguous nucleic acid sequence from between position 7 and position 2691 of SEQ ID NO:28; from between position 7 and position 2628 of SEQ ID NO:30; from between position 7 and position 2559 of SEQ ID NO:32; from between position 7 and position 2502 of SEQ ID NO:34; from between position 7 and position 2349 of SEQ ID NO:36; from between position 7 and position 2559 of SEQ ID NO:38; from between position 7 and position 2697 of SEQ ID NO:40; from between position 7 and position 2583 of SEQ ID NO:42; from between position 7 and position 2397 of SEQ ID NO:44; from between position 7 and position 2613 of SEQ ID NO:46; from between position 7 and position 2619 of SEQ ID NO:48; or from between position 7 and position 2790 of SEQ ID NO:50.

45 (new). A DNA segment comprising an isolated gene encoding for a modified retinoblastoma tumor suppressor protein, said protein consisting of the contiguous amino acid sequence of SEQ ID NO:29; SEQ ID NO:31; SEQ ID NO:33; SEQ ID NO:35; SEQ ID NO:37; SEQ ID NO:39; SEQ ID NO:41; SEQ ID NO:43; SEQ ID NO:45; SEQ ID NO:47; SEQ ID NO:49; or SEQ ID NO:51.

46 (new). A recombinant vector comprising the DNA segment of claim 44.

47 (new). A pharmaceutical composition comprising the DNA segment of claim 44 and a pharmaceutically acceptable excipient.

48 (new). A pharmaceutical composition comprising the recombinant vector of claim 46 and a pharmaceutically acceptable excipient.